ETHIOPIAN FOOD AND DRUG AUTHORITY

GUIDELINE FOR RELIANCE AND JOINT CLINICAL TRIAL OVERSIGHT

Document No.	Version No	Approval Date	Issue Date
EFDA/GDL/78	001	12/06/2025	18/06/2025

Document History

Version No.	Reason for Amendment	Effective Date
001	Newly issued document	18/06/2025

Asnakech Alemu,

Pharmacovigilance and Clinical Trial Lead Executive Office

Foreword

In an increasingly interconnected world, the need for robust and harmonized regulatory frameworks has never been more critical. The reliance and joint review guidelines represent a significant step forward in fostering collaboration among regulatory authorities, ensuring that medical products are safe, effective, and of the highest quality.

These guidelines are designed to foster cooperation among regulatory authorities, streamline the approval process, and ensure that clinical trials are conducted to the highest standards of safety and efficacy. By leveraging the collective expertise and resources of multiple regulatory bodies, we can reduce duplication of efforts and accelerate the availability of life-saving treatments.

The development of these guidelines has been a collaborative effort, involving input from diverse group of stakeholders, including regulatory authorities, industry representatives, and public health experts. We extend our gratitude to all those who have contributed their time and expertise to this initiative.

I am confident that these guidelines will serve as a valuable resource for regulatory authorities and the pharmaceutical industry, promoting greater consistency and transparency in clinical trial oversight. Together, we can ensure that patients have timely access to safe and effective medical treatments.

I would like to extend my heartfelt gratitude to all experts including clinical trial researchers, ethics committee members and Technical Working Group (TWG) members who have directly or indirectly contributed their expertise to the revision of this guideline. I invite all interested parties to continue showing their support by sharing their feedback and suggestions with the EFDA at P.O.Box 5681 Addis Ababa, Ethiopia, or by reaching out via telephone at 251-115524122 or email at *contactefda@efda.gov.et.*

Heran Gerba
Director General
Ethiopian Food and Drug Authority

Acknowledgements

The Ethiopian Food and Drug Authority (EFDA) extends its sincere appreciation to all workshop participants and contributors to the development of this Guideline for Reliance and Joint review Clinical Trial Oversight. We also extend our heartfelt gratitude to the TWG members for drafting, presenting the document to workshop participants, and refining it by incorporating the forwarded comments.

Technical Working Group Members

S.no	Name of Participants	Position	Institution
1.	Prof. Ephrem Engidawork	CTA advisory committee	AAU
2.	Prof. Ariaya Hymete	CTA advisory committee	AAU
3.	Mr. Assefa Ejamo	Clinical Trial Authorization Desk Head	EFDA
4.	Dr. Yalemzewid Ankela	Clinical Trial Authorization and GCP Inspection Expert	EFDA
5.	Mr. Abera Mulatu	Clinical Trial Authorization and GCP Inspection Expert	EFDA
6.	Mr. Abebe Telila	Clinical Trial Authorization and GCP Inspection Expert	EFDA
7.	Dr. Zelalem Aysheshim	Clinical Trial Authorization and GCP Inspection Expert	EFDA
8.	Mrs. Hiwot Getachew	Clinical Trial Authorization and GCP Inspection Expert	EFDA
9.	Mr. Workagegnew	Pharmacovigilance	EFDA
10.	Mr. Demeke	Pharmacovigilance	EFDA
11.	Mrs. Mihret Maru	Pharmacovigilance	EFDA
12.	Mr. Habtamu Gashaw	Pharmacovigilance	EFDA

Table of Contents

Abbreviations and Acronyms

AMA	Africa Medicine Agency
AVAREF	African Vaccine Regulatory Forum
CROs	Clinical Research Organizations
CAPA	Corrective Action and Preventive Action
CRFs	Case Report Forms
CTAs	Clinical Trial Applications
EFDA	Ethiopian Food and Drug Authority
EMA	European Medicine Agency
EU	European Union
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
ICH	International Council for Harmonization
IECs	Institutional Ethics Commitees
IGAD	Intergovernmental Authority on Development
MA	Marketing Authorization
MEMA	Medicine Evaluation and Market Authorization
MoUs	Momurandum of Understandings
NRAs	National Regulatory Authority
QC	Quality Control
REC	Regional Economic community
RRAs	Reference Regulatory Authorities
SOP	Standard Operating Procedure
TOR	Terms of Reference
TWG	Technical Working Group
WHO PQ	World Health Organization Pre-qualification

Guideline for Reliance and Joint Clinical Trial Oversight

1. Background

The Ethiopian Food and Drug Authority (EFDA) is mandated by Proclamation No. 1112/2019 to ensure that all Medical products approved and made available in the market meet the prescribed standards of quality, safety and efficacy. Article 27 (sub articles 2 and 4) of this proclamation decrees that "The executive organ shall authorize clinical trial on human subjects only after the clinical trial protocol is evaluated and accepted from scientific, legal and ethical perspectives, and may require review and monitoring of the approved clinical trial study by an appropriate national, regional or institutional review organ". Thus, EFDA is continuously working to improve the clinical review and authorization of investigational drugs to ensure safety, ethics, and data integrity. To this effect, EFDA has developed various tools, including legal frameworks, guidelines, directives, and use of risk-based approaches in regulatory clinical trial oversight activities such as good clinical practice (GCP) inspections and stringent protocol review.

Despite the significant steps taken by EFDA to boost clinical trial investigations and improve the regulatory environment, the number of applications submitted and trials conducted in the country are still limited. An effort made to come up with a strategy to mitigate this and other challenges in the regulatory landscape brought forward the concept of reliance. This approach enables national regulatory authorities (NRAs) to leverage the work performed by other trusted authorities in their regulatory decision the face of this, reliance is emerging as a practical approach of regulatory decision making. Indeed, reliance has been shown to increase regulatory capacity and efficiency. This would undoubtedly facilitates the evaluation of clinical trial applications addressing diseases of public health importance, thereby improving the access of drug products for public health emergencies, rare diseases, and emerging and re-emerging infectious diseases of public health threats.

Another approach to facilitate clinical trial authorization is joint clinical trial review. This is a collaborative process where different organizations, such as regulatory bodies, invited experts, and clinical trial applicants come together to assess the design, execution, and outcomes of a clinical trial. This review typically aims to ensure that the trial adheres to ethical standards, regulatory requirements, and scientific rigor. It may involve discussions on trial protocols, data integrity, patient safety, and the efficacy of the intervention being tested. Joint review may also help identify potential risks, address challenges, and offer recommendations for improving trial methodology

or reporting. The joint effort can facilitate a more comprehensive evaluation of the trial and ensure that it meets both local and international standards for clinical research. Outcomes can be maximized when joint clinical trial review is complemented with a joint GCP inspection. This task is a collaborative process where regulatory authorities from multiple countries conduct inspections to ensure compliance with GCP standards during clinical trials. These inspections aim to verify that the rights, safety, and well-being of trial participants are protected, and that the data generated from the trial are credible and reliable.

In view of the extent and complexity of the regulatory challenges, establishing and maintaining a mature regulatory system will require adequate resources, including skilled, capable human resources and a significant financial investment. Thus, EFDA promotes innovative and more effective forms of collaboration that optimize resources, thereby enhancing clinical trials in Ethiopia. Thus, the Authority will engage in reliance, joint review, and joint inspection endeavour, as deemed necessary, with other regulatory authorities to step up regulatory efforts. To this effect, this guideline is developed to direct how such collaborations are effected.

2. Definitions

Abridged regulatory pathway: regulatory procedures facilitated by reliance, whereby a regulatory decision is made solely or partially based on application of reliance.

Clinical Research Organization: a person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of sponsors trial related duties and functions.

Expedited review: refers to reviewing and approving clinical trials following a fast-track or non-routine procedure during public health emergencies, addressing public health interest, or where access to new therapies needs to be made faster than the routine timelines to save or dramatically improve patients' lives are necessary.

Harmonization: Refers to a process where the ethical and regulatory standards, requirements, procedures, or practices governing clinical trials are consistent across different countries, regions or institutions.

Multi-country clinical trial: a clinical trial conducted in more than one country under a single protocol.

Multi-Regional Clinical Trial: refers to a clinical trial conducted in more than one country/region under a single protocol.

Public health emergency: refers to an occurrence or imminent threat of an illness or health condition that is caused by appearance of a novel or previously controlled or eradicated infectious agent or biological toxin; a natural disaster; a chemical attack or accidental release; and an attack or accidental release of radioactive materials, and poses a high probability of deaths, serious injuries or long-term disabilities to a large number of people.

Public health threat: refers to any situation or factor that may represent a danger to the health of the people.

Rare disease: refers to disorders such as inherited metabolic disorders and other diseases with similar rare occurrence but excluding catastrophic (i.e., life threatening, seriously debilitating, or serious and chronic) forms of more frequently occurring diseases.

Recognition: is a routine acceptance of the regulatory decision of another regulator or trusted institution. Recognition indicates that evidence of conformity with the regulatory requirements of a country is sufficient to meet the regulatory requirements of another country.

Reference regulatory Authority: a stringent regulatory authority or trusted institutions whose regulatory decisions are relied up on by another regulatory authority to inform its own decision.

Regulatory Reliance: an act whereby the EFDA considers and gives significant weight to assessments performed by another NRA or trusted institution or recognized regulatory authority, or to any other authoritative information in reaching its own decision. The relying authority remains independent, responsible and accountable for the decisions taken, even when it relies on the decisions, assessments and information of others.

Regulatory review: a process that ensures the technical and scientific soundness, merit, and regulatory compliance of a clinical trial application.

Reliance pathways: an alternative non-routine authorization pathways used by the authority in its regulatory decisions regarding clinical trial application based on assessment outcomes of recognized regulatory authority (ies) or institutions.

Sponsor: an individual, company, institution, or organization, which takes responsibility for initiation and/or financing of a clinical trial.

Work-sharing: is a process by which the regulatory authority of two or more regulatory authority shares activities, including joint reviews and joint inspection, to accomplish a clinical trial regulatory task.

Verification: is a process of confirming that the regulatory decisions or assessments from a reference regulatory authority and international organization such as WHO, AVAREF are applicable, relevant, and valid for the local context, before accepting or using them in whole or in part for regulatory decision-making.

3. Objectives

3.1. General objective

The objective of this guideline is to provide direction on the implementation of reliance and joint clinical trial oversight to promote a more efficient and effective approach in regulatory decision making.

3.2. Specific objectives

- To provide guidance to applicants regarding EFDA's reliance procedures on clinical trial oversight
- To provide mechanisms for coordination and cooperation of EFDA with other regulatory authorities regarding clinical trial oversight.

4. Scope

This guideline covers mechanisms to undertake joint review and inspection of clinical trial endeavors taking into account the concept of reliance. The guideline will be applicable to institutions, including NRAs, Institutional Ethics Committees (IECs), Clinical Research Organizations (CROs), and regional and international organizations.

5. Reliance

5.1. Principles of good reliance practice

The principle of reliance in this guideline is to optimize innovative and more effective forms of collaboration in order to make the best use of available resources and expertise, and avoid duplication of efforts to ensure the safety, quality and efficacy of medicinal products. The following reliance principles will apply.

1. **Sovereignty:** the Authority reserves the right to decide when and how to use reliance and in which circumstances. EFDA retains its prerogative to assess applications and apply judgments that consider benefits and risks as it applies to the Ethiopian context.
2. **Legal basis:** reliance procedures are coherent with the national legal frameworks.
3. **Transparency:** the reliance approach remains transparent regarding laws, requirements, regulatory systems and processes to be followed as well as the rationale for relying on a specific entity should be disclosed and understood by all parties.
4. **Competency:** reliance requires that national authorities build the necessary competencies for critical decision making as well as for proper implementation. The competencies are bench-marked by transparent processes that develop trust on the capacities of recognized regulatory authorities.

5. **Consistency:** the decision-making process in clinical trial authorization is predictable and applied uniformly across similar circumstances, ensuring fair and reliable outcomes for public health.

5.2. Criteria for reliance applications

The clinical trial application, with a similar protocol and the same investigational product information submitted to the Reference Regulatory Authorities (RRAs) for reliance, should meet at least one of the following criteria.

- Multi-country trials
- Trials with public health importance,
- Public health emergencies,
- Rare diseases
- Emerging and re-emerging infectious diseases of public health threats
- Submission should be made within one year following approval by an RRA

5.3. Requirement for selection of Reference regulatory Authority or trusted Institutions

Regulatory authorities or institutions shall fulfil at least the following criteria to be included in the list of EFDA recognized reference regulatory authorities/trusted institutions. The criteria can be updated on regular bases based on the authority priorities or emerging regulatory conditions

- Stringent regulatory authority, regional (AVAREF and AMA) or WHO Maturity Level 3 bench-marked regulatory authorities.
- A regulatory authority associated with an ICH member through a legally binding, mutual recognition agreement,
- National regulatory authority or institution that has signed memorandum of understanding (MoU), legally binding agreement, and common harmonized documents (i.e., guidelines, regulatory requirements…) with authority.

5.4. Reliance pathways

The authority employs reliance pathways in its regulatory decisions to accelerate the approval of clinical trial applications (CTAs) and monitoring decisions. The reliance aims to reduce timelines compared to standard regulatory practices, but the authority shall remain responsible and accountable for the decisions taken. Regulatory reliance can follow either of the following approaches:

- **Verification:** is an administrative process for taking a regulatory decision, based on the authorization

of a clinical trial by any Reference Regulatory Authority. It can also be applied when conformity of the protocol with the requirements of the RRA are sufficient to meet the requirements of EFDA or if EFDA has harmonized its working processes with NRAs that have similar WHO bench-marking level.

- **Abridged review**: may pertain to the full submission or parts thereof of the protocol, depending on the suitability of use under local conditions and regulatory requirements. The evaluation of a certain part of the application such as assessment of the benefit-risk of using the investigational drug in the local ethnic population, medical practice/culture, patterns of disease and nutrition may be conducted.

5.5. The practice of reliance

5.5.1. Clinical trial authorization:

EFDA's reliance on clinical trials involves receiving the application followed by implementation of the reliance mechanisms as appropriate.

- **Submission of the protocol and protocol supplement:** the approved version of clinical trial protocol and associated documents including reliance application, Authorization/Approval letter from RRA, investigator brochures, informed consent forms translated to local language, RRA's review summary and sponsors response (EFDA will accept only full fledged review outcome), and any other relevant documents; (http://www.efda.gov.et/doc-category/clinical-trials/) should be submitted to EFDA.
- **Screening:** the application will be checked for complete submission of the required documents to determine the reliance pathway. Screening will be completed within 4 working days.
- **Review:** The review process will start after complete submission of the required documents and service fee payment. The clinical trial reliance application review process will follow either of the two pathway;
    - **a. Verification**: if the application is approved by an RRA, the following documents will be verified during the review process; translated patient information sheet/consent, site agreement, trial staff profile, sponsor/country PI agreement, conflict of interest disclosure, and national ethical approval letter. The authorization will be issued within 5 working days.
    - b. **Abridged review**: an application is subjected to abridged review if it is believed to pose a risk for the local study participants. RRA's review summary and sponsors response can be used as a basis to determine the extent of the review. The abridged review will be completed within 10 working days.

5.5.2. Clinical trial monitoring

The authority will exchange clinical trial monitoring reports or decisions, including GCP inspection decisions, safety reports, and other relevant clinical trial related information with RRAs. The information shared from the RRAs will be evaluated by the authority for taking appropriate actions.

6. Joint Review

This is a task shared between two or more regulatory authorities inlcluding IECs. Joint review is intended to enhance the quality of the review of an application submitted to multiple countries, optimize review timelines for such applications, serve as a platform to allow regulators and IECs to exchange and validate their findings with peers and also act as a capacity-building tool. Through joint review, regulators of participating countries review and exchange thoughts together and speed up the CTA review process. Joint review can be done as a regular and expedited review. Expedited review can be performed for clinical trials involving life-threatening conditions, availability of data for unmet medical need, and expected benefit outweighs the risk.

6.1. Prerequisites for joint review

The following are important prerequisites for the successful conduct of joint reviews:

- There should be MoU signed between EFDA and other participating countries or independent ethics committee.
- There should be a harmonized tool(s) and generate a common report as a basis for national decision to authorize a trial.
- A coordinating country/institution should be selected by the collaborating countries/institutions
- All applicable fees should be paid in advance.
- Reviewers should be nominated by the collaborating countries/institutions
- Reviewers should be culturally sensitive
- The protocol and protocol supplement should be submitted in advance.
- Invited experts, if any, will only provide their expertise recommendations

6.2. Criteria for joint review

A candidate medical product of high public health value to participating countries will be considered for joint review based on the following criteria and the clinical trial application for joint review should meet at least one of the following criteria:

- Addresses a neglected tropical disease, rare diseases, unmet medical need or other highly prevalent and serious diseases in the participating countries.
- Involves a novel technology
- Product that addresses a disease for Public Health Emergency of International Concern (PHEIC).
- For high-risk clinical trials as defined by NRA
- When the clinical trial is a multi country trials
- Request from one or more countries for assistance.

6.3. Joint review process

A proactive approach to the conduct of joint reviews will be established, including online expressions of interest. The process can also involve a concurrent or sequential review of the protocol by the collaborating NRA followed by a joint assessment session to finalize the review. A team can also be set up between the collaborating institutions/NRAs to review and finalize the report.

A request for a joint review can be initiated by various entities, including sponsors, AVAREF, AMA, the IGAD Medicine Harmonization initiative, or any collaborating countries/Institutions that has MoUs with EFDA, WHO, or other international organizations, as well as EFDA itself.
The joint review process will be as follows;

Step 1- Screening of requests

Request of the joint review application will be received by EFDA and screened by internal technical working group.

Step 2 - Pre-submission meeting

Organized by the EFDA or requesting country/agency in discussion with the applicant, participating countries and the neutral partner (if involved). The objective is to present general information about the investigational product, the clinical trial plan, and proposed timelines. A decision is made on whether to proceed with a joint review in accordance with working document or guideline of participating countries. A date and location for the face to face meeting can also be set. Participating countries will decide on their participation and commit to nominate reviewers.

Step 3 - Submission to countries

The applicant will submit the applications to the participating countries as agreed during the pre-

submission meeting. The trial applications will be first screened by participating countries to assess completeness of the submitted documents. The clinical trial application is not considered valid until all administrative requirements are fulfilled (including the payment of fees, if passed screening). Opportunities for central electronic filing of application and subsequent access by the countries will be explored.

Step 4– Country review

Once the application has passed the screening/validation step, the reviewers will upload their feedback on the joint review platform. Comments will be accessible to all joint review participants, including the applicant.

Step 5– Joint review

EFDA or the requesting country/agency will organize the joint review meeting at the agreed upon date and location. Depending on the complexity of the review, working days will be allotted for the review. The host will circulate an agenda for the meeting. The structure of the meeting will generally have the following format:

Opening session (all participants):

Host's role:

- Objectives of the meeting, agenda and expected outcomes
- Disclosure of conflict of interest
- Elect chair(s) and rapporteur(s) for the meeting

Applicant's role:

Provides responses to queries raised by countries to which the application was submitted.

Closing session (all participants):

The questions and answers sessions will continue until all questions are either completely resolved or agreements reached on a list of outstanding questions to addressed by the applicant. In the former case, the review report will be finalized and signed by the Chair(s), countries and applicant. In the latter case, the sponsor submits pending responses to each participating country or agency. Participants in the joint review will then review and communicate virtually to ensure consistency and reach consensus on resolution of the questions jointly presented to the applicant. If they agree that the questions were not

satisfactorily responded to, the applicant will be requested to provide additional information. The process will continue until all participating countries agree that the questions have been satisfactorily resolved.

Step 6- National Decision

After the joint review as described above has been completed, each participating countries will proceed to issue the decision according to their national procedure.

Step 7 – Post-authorization

Countries are encouraged to coordinate and streamline timely authorization of importing investigational products so that near simultaneous commencement of trials in the respective countries could be possible.

Table 1: Timeline for the joint review process

Step	Description	Target Timeline (working days)		Responsibility
		Regular	Expedited	
1	Screening of requests for a joint review	5	2	Participating country
2	Pre-submission meeting	1	1	Hosting country /agency
3	Submission to NRA by applicant	2	1	Applicant
4	Screening by the NRA	5	2	Participating countries
5	Country review	22	11	Participating countries
6	Joint review	3-10	2-5	Participating countries
7	National decision	5	2	Participating countries
8	Post-authorization (the start of the trial to begin, including the authorization to import investigational medical products)	6	10-30	Participating country

7. Joint Good Clinical Practice Inspection

Involves a collaborative on-site or remote inspection of a clinical trial facility conducted by multiple regulatory authorities, working together to assess the site's compliance with GCP standards and ensure participants right and safety as well as integrity of the data generated.

7.1. Prerequisites for joint inspection

The following are important pre-requisites for a joint GCP inspection

- An authorized clinical trial involving more than one country or a country in case of assisted inspection.
- Consensus among the countries involved to undertake GCP inspection together utilizing a harmonized tools and to use a common report as a basis for their national decision. To this effect, an MoU should be signed between the participating countries.
- A written agreement obtained from the applicants to support the conduct of joint GCP inspection by each participating country.
- Trained and experienced GCP inspectors nominated by the heads of agencies from each participating country.
- All applicable fees should be paid in advance

7.2. Criteria for joint GCP inspection

In principle, a CTA jointly reviewed by participating countries is eligible for joint GCP inspection. However, there could be instances where countries seek support in GCP inspection without involving other countries in the review process. In both situations, the criteria used for joint review are still applicable for joint GCP inspection. Apart from that, the following criteria can be added.

- Participating countries in the joint GCP inspection must agree on the GCP related activities in terms of roles, responsibilities, process, and timelines.

7.3. Joint GCP Inspection process

- Detail terms of reference or proposal regarding the joint GCP inspection shall be prepared and endorsed by each participating country
- Detail of site to be inspected (name of site, full addresses, telephone and email addresses) shall be communicated in advance among participating countries
- The GCP inspection shall be carried out in accordance with international ethical and scientific quality standard, authorized protocol, local rules and regulations

- Each participating country shall assign at least two GCP inspectors, And the lead inspector shall be delegated from the inspection team based on mutual agreement.
- The joint GCP inspection shall be carried out either on site or remote based on the mutual agreement of the participating country.
- The inspection will be announced to the sponsor/applicant in writing and additional documents/information will be requested by the respective regulatory authority if necessary.

7.4. Process steps

7.4.1. Planning and Coordination

- **Initiation**: NRAs, sponsors, or regional/international bodies can identify the need for a joint inspection.
- **Collaboration Agreement**: stakeholders agree on the scope, objectives, and roles of participating agencies.
- **Team Selection**: Inspectors from each agency are selected, considering expertise relevant to the trial's focus.
- **Timeline and Logistics**: a mutually agreed timeline, inspection agenda, and logistics (e.g., travel, confidentiality agreements) are established.

7.4.2. Preparation

- **Document Review**: Inspectors review the clinical trial protocol, investigator's brochure, ethics committee approvals, and prior inspection reports. Evaluate critical data related to good clinical practice (GCP) compliance and patient safety.
- **Risk Assessment**: Identify key risk areas or concerns based on the trial's design, previous findings, or known issues.
- **Pre-Inspection Meeting**: Stakeholders hold a meeting to align on objectives, methodologies, and communication strategies during the inspection.

7.4.3. On-Site Inspection

- **Facility Tour**: Inspectors examine facilities, equipment, and infrastructure for compliance with GCP and applicable regulations.
- **Document Verification**:Review essential trial documents, including informed consent forms, source data, and case report forms (CRFs). Cross-check records for consistency and compliance.

- **Interviews**:Conduct interviews with investigators, study coordinators, and other staff. Assess their understanding of trial procedures, protocol deviations, and reporting responsibilities.
- **Data Review**: Verify accuracy, integrity, and completeness of collected trial data. Check adherence to monitoring plans and data management protocols.

7.4.4. Collaboration and Interim Reporting

Inspectors discuss findings, interpretations, and observations as they occur. Collaboratively identify any deficiencies or areas of non-compliance. Summarize daily findings among the joint inspection team to align perspectives.

7.4.5. Post-Inspection Activities

- **Report Compilation:** each agency drafts its observations and findings. A consolidated joint inspection report is created, highlighting areas of compliance and non-compliance.
- **Sponsor/Investigator Response**:The clinical trial team is required to address deficiencies through a corrective and preventive action (CAPA) plan.
- **Regulatory Decision**: NRAs decide on the trial's continuation, amendments, or termination based on inspection findings.

7.4.6. Follow-Up

- **Verification**: Inspectors verify that corrective actions have been implemented effectively.
- **Documentation**: Maintain detailed records for regulatory archives and future reference.
- **Feedback**: Share lessons learned and insights to improve future joint inspections.

8. Regulatory and Ethical Harmonization

Harmonizing regulatory and ethical frameworks for clinical trials is crucial for efficient and ethical research globally, particularly in the context of multinational trials and emerging regulatory conditions. It aims to streamline review processes, reduce burdens and ensure consistent ethical and regulatory standards across different regions, countries, and institutions.

- The authority will standardize and harmonize working documents with collaborating countries/institutions to facilitate the reliance and joint clinical trial oversight activities
- The procedures or relevant guidelines should be established compliance to this guideline
- EFDA can establish specific Guidelines or procedures such as Terms of Reference (ToR), MoU or Standard Operating Procedures (SOPs) to work with any interested country and IECs

This guideline can be amended as deemed necessary. The MoU signed between the participating countries is drafted by the initiating country.

Reference

1. EFDA Guidelines on Reliance for Regulatory Decision Making.pdf, December, 2022
2. Philippines Guidelines on Regulatory Reliance on the Conduct of Clinical Trials in Philippines.pdf
3. AVAREF Guideline for Reliance, December, 2022
4. TRS 1033 - Annex 10: Good reliance practices in the regulation of medical products: high level principles and considerations

Annex I: List of Reference NRAs or institutions

The list of NRA and Institutions considered as reference regulatory authority or trusted institution for reliance for clinical trials.

NMRA/Institution	**Country**
1. US FDA	USA
2. Therapeutic Goods Administration (TGA)	Australia
3. The Austrian Medicines and Medical Devices Agency (AGES MEA)	Austria
4. Federal Agency for Medicines and Health Products (FAMHP)	Belgium
5. Health Canada	Canada
6. Danish Medicine Agency	Denmark
7. Finnish Medicine Agency	Finland
8. National Agency for Safety of Medicines and Health Products (ANSM)	France
9. The Federal Institute for Drugs and Medical Devices (BfArM)	Germany
10. Health Products Regulatory Authority (HPRA)	Ireland
11. Italian Medicine Agency (AIFA)	Italy
12. Pharmaceuticals and Medical Devices Agency (PMDA)	Japan
13. Medicine Evaluation Board	Netherlands,
14. Norwegian Medical Products Agency (NOMA)	Norway
15. Swiss Agency for Therapeutic Products (Swissmedic)	Switzerland
16. Medicines and Health Products Regulatory Agency (MHRA)	United Kingdom
17. Regional economic communities (RECs) operating under the umbrella of African Medicine Agency where joint assessment conducted (such as IGAD) and AMA joint assessment	IGAD-AMA
18. Bulgarian Drug Agency	Bulgaria
19. Agency for Medicinal Products and Medical Devices of Croatia (HALMED)	Croatia
20. Ministry of Health — Pharmaceutical Services	Cyprus
21. State Institute for Drug Control (SUKL)	Czech Republic
22. State Agency of Medicines (Ravimiamet)	Estonia

23. National Organization for Medicines	Greece
24. National Institute of Pharmacy and Nutrition (OGYEI)	Hungary
25. Icelandic Medicines Agency	Iceland
26. State Agency of Medicines	Latvia
27. Office of Health / Department of Pharmaceuticals	Liechtenstein
28. State Medicines Control Agency (VVKT)	Lithuania
29. Ministry of Health	Luxemburg
30. Medicines Authority	Malta
31. Chief Pharmaceutical Inspectorate	Poland
32. National Authority of Medicines and Health Products (Infarmed)	Portugal
33. National Agency for Medicines and Medical Devices	Romania
34. State Institute for Drug Control (SIDC)	Slovakia
35. Agency for Medicinal Products and Medical Devices (JAZMP)	Slovenia
36. Spanish Agency of Medicines and Medical Devices (AEMPS)	Spain
37. Medical Products Agency	Sweden
38. WHO AVAREF	
39. EMA	
40. In addition to these countries ML4 and ML 3 WHO attegned countries are considered	

Annex 2: Reliance Application Form for Clinical Trial Authorization

A. RELIANCE APPLICATION GENERAL INFORMATION	
Clinical Trial Title	
Short title (Acronym) if applicable	
Unique Identifier (Application ID)	
Protocol No.	
Version No.	
Investigational product	
Date of Application	
Submitted to	
B. Reliance Applicant Information	
Applicant Type: (Check one) ☐ Sponsor ☐ Principal Investigator ☐ Contract Research Organization (CRO) on behalf of sponsor ☐ Other (Specify): _____	
Sponsor Name: (Full legal name)	
Sponsor Contact Person: (Name, title)	
Sponsor Phone Number:	
Sponsor Email:	
Principal Investigator Name: (If different from sponsor)	
Principal Investigator Affiliation/Institution:	
Sponsor Address: (Physical address)	
Principal Investigator Contact Information: (Phone, email)	
CRO Name: (If applicable)	
CRO Address	
CRO Contact Person:	
CRO Phone Number:	
CRO Email:	
***C.* CLINICAL TRIAL INFORMATION**	
Clinical Trial Title: (Full title as per the protocol)	
Clinical Trial Protocol Number:	
Investigational Product (IP) Name: (Generic/Brand Name)	
IP Dosage Form:	

IP Strength:	
IP Indication/Intended Use:	
Study Phase: (e.g., Phase I, II, III, IV)	
Planned Number of Participants in [Your Jurisdiction]	
Planned Number of Participants Globally:	
Primary Endpoint(s):	
Brief Summary of Study Design:	
Trial Duration: (Estimated Start Date - Estimated End Date)	
Trial Location(s): (All study locations)	

D. Reliance Information

Request for Reliance: (Check one) ☐ Yes, we are applying for reliance. ☐ No, we are not seeking to apply under the reliance pathway. If No, provide a brief explanation why the reliance route is not being used _____	
Name of the Trusted Regulatory Authority (TRA) whose assessment is being relied upon:	
If more than one TRA, list them all.	
Official Authorization/Approval Number from the TRA(s): (Include reference/registration number(s) with date)	
Date of TRA Approval/Authorization: (For each authority if more than one)	
Type of Decision or Document for Reliance (Check all that apply): ☐ Authorization for the Clinical Trial ☐ Clinical Trial Assessment Report ☐ Inspection Report ☐ WHO Pre-qualification Status ☐ Other (Specify): _____	
Has the protocol submitted to the TRA(s) been modified? ☐ Yes (Provide details of the differences) ☐ No	
Is there a material difference between the investigational product submitted to the TRA, and the investigational product being used in your clinical trial? ☐ Yes (Provide details of the differences) ☐ No	
SUPPORTING DOCUMENTATION (CHECKLIST)	
Please provide the following documents and check the box once they have been	

included: ☐ Cover Letter indicating intent to use reliance pathway and a rationale for why reliance is appropriate. ☐ Copy of authorization letter/approval from the trusted regulatory authority (TRA). ☐ Complete Assessment Report(s) from the TRA(s). ☐ Complete Inspection Report(s) from the TRA(s) (if applicable) ☐ Copy of the WHO Prequalification Certificate(if applicable). ☐ Complete copy of the clinical trial protocol. ☐ Copy of the Investigator's Brochure (IB). ☐ Copy of the Informed Consent Form (ICF) that will be used at your site. ☐ Documentation demonstrating GCP compliance at study sites. ☐ Declaration that the clinical trial protocol and investigational product are substantially the same as those approved by the trusted regulatory authority (TRA). ☐ Summary of Product Dossier and safety data, as well as information on the IMP. ☐ Details of any proposed changes or adaptations to the original protocol, including justification for any changes being made. ☐ Any other supporting documentation to support the reliance decision, as required by your regulatory authority.	
DECLARATIONS	
Applicant Declaration: "I/We, the undersigned, declare that all information provided in this application and the accompanying documentation is true, accurate, and complete to the best of my/our knowledge. I/We further declare that the clinical trial will be conducted in compliance with all applicable laws, regulations, and ethical guidelines in EFDA. I/We further declare that I/We understand that all requirements laid out in the EFDA's SOPs for Regulatory Reliance must be followed. Name of Declarant: _____ Title of Declarant: _____ Signature: _____ Date: _____	